CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
20-920

Microbiology Review(s)

REVIEW TO HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF/HFD-805
MICROBIOLOGY REVIEW #4 OF NDA

14 February 2001

A. 1. NDA: 20-920/AZ

2. TYPE OF SUPPLEMENT: N/A

3. SUPPLEMENT PROVIDES FOR: N/A

4. APPLICANT/SPONSOR: Scios, Inc.
820 West Maude Ave
Sunnyvale, CA 94085

5. MANUFACTURING SITE: [redacted]

6. DRUG PRODUCT NAME:
Proprietary: Natrecor®
Nonproprietary: nesiritide
Drug Priority Classification:

7. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Lyophilized powder, 1.5 mg in a 5 mL vial, for IV Infusion

8. METHOD(S) OF STERILIZATION: [redacted]

9. PHARMACOLOGICAL CATEGORY: Anti-Arrythmic

B. 1. DOCUMENT/LETTER DATE: April 24, 1998
2. RECEIPT DATE: January 10, 2001
3. CONSULT DATE: January 11, 2001
4. DATE OF AMENDMENT: January 9, 2001
5. ASSIGNED FOR REVIEW: January 22, 2001
6. SUPPORTING/RELATED DOCUMENTS: Previous Microbiology reviews of 20-920 dated 8/12/98; 12/1/98; and 3/25/99.

C. REMARKS: The original NDA was recommended for approval from a product quality microbiology standpoint (3/25/99). This amendment covers changes made to the manufacturing process since that recommendation.

D. CONCLUSIONS: This submission is recommended for approval on the basis of product quality microbiology.

/S/

Bryan S. Riley, Ph.D.
Microbiology Reviewer

cc.: Original NDA 20-920
HFD 110/Division File
HFD 110/Project Manager
HFD 110/Other
HFD 805/Consult File
HFD 805/ B. Riley

Drafted by: Bryan Riley, Ph.D.
R/D initialed by: Peter Cooney, Ph.D.

Redacted 5

pages of trade

secret and/or

confidential

commercial

information

D Willard

REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

APR 8 1999

Microbiologist's Review #3 of NDA 20-920/BC
March 25, 1999

A. 1. **APPLICATION NUMBER:** 20-920/BC

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. **PRODUCT NAMES:** Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. **METHOD(S) OF STERILIZATION:** [ ]

5. **PHARMACOLOGICAL CATEGORY:** Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. **DATE OF INITIAL SUBMISSION:** April 24, 1998

2. **AMENDMENT:** October 2, 1998 and March 11, 1999

3. **RELATED DOCUMENTS:**

4. **ASSIGNED FOR REVIEW:** March 22, 1999

5. **DATE OF CONSULT REQUEST:** March 16, 1999

C. **REMARKS:**

The amendment provides for responses to "List of Microbiology Comments and Deficiencies" in Microbiologist's Review #2.

D. CONCLUSIONS:

The submission is recommended for approval for issues concerning microbiology.

/S/ — 3/25/99

Brenda Uratani, Ph.D.
Review Microbiologist

Date 3/25/99

cc:

NDA 20-920 /BC
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 3/25/99
R/D initialed by P. Cooney, 3/25/99

D. Willard

REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

AUG 13 1998

Microbiologist's Review #1 of NDA 20-920
August 12, 1998

A. 1. **APPLICATION NUMBER:** 20-920

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. **PRODUCT NAMES:** Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. **METHOD(S) OF STERILIZATION:** [ ]

5. **PHARMACOLOGICAL CATEGORY:** Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. **DATE OF INITIAL SUBMISSION:** April 24, 1998

2. **AMENDMENT:**

3. **RELATED DOCUMENTS:**

4. **ASSIGNED FOR REVIEW:** May 1, 1998

5. **DATE OF CONSULT REQUEST:** June 10, 1998

C. **REMARKS:**

Human B-type natriuretic peptide (hBNP), a 32-amino acid peptide, is produced as a fusion protein in *Escherichia coli*. The fermentation and manufacture of the drug substance are performed in [ ] The manufacture of the drug product is conducted at [ ]

D. CONCLUSIONS:

The submission is approvable pending on resolution on container-closure integrity issue. Specific comments are provided in "Review Notes" and in the "List of Microbiology Deficiencies and Comments".

/S/ 8/12/98

Brenda Uratani, Ph.D.
Review Microbiologist

Pik 8/12/98

cc:

NDA 20-920
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 8/12/98
R/D initialed by P. Cooney, 8/12/98

Redacted 8

pages of trade

secret and/or

confidential

commercial

information

D. Hazel

REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

DEC 1 1998

Microbiologist's Review #2 of NDA 20-920/BI
December 1, 1998

A. 1. **APPLICATION NUMBER:** 20-920 /BI

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. **PRODUCT NAMES:** Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. **METHOD(S) OF STERILIZATION:** [ ]

5. **PHARMACOLOGICAL CATEGORY:** Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. **DATE OF INITIAL SUBMISSION:** April 24, 1998

2. **AMENDMENT:** October 2, 1998

3. **RELATED DOCUMENTS:**

4. **ASSIGNED FOR REVIEW:** October 26, 1998

5. **DATE OF CONSULT REQUEST:** October 5, 1998

C. **REMARKS:**

The amendment provides for responses to "List of Microbiology Comments and Deficiencies" in Microbiologist's Review #1.

D. CONCLUSIONS:

The response to Microbiology deficiency is not satisfactory. The submission is approvable pending on resolution on container-closure integrity issue. Specific comments are provided in "Review Notes" and in the "List of Microbiology Deficiencies and Comments".

/S 12/1/98

Brenda Uratani, Ph.D.
Review Microbiologist

cc:

NDA 20-920 /BI
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 12/1/98
R/D initialed by P. Cooney, 12/1/98

/S for PHC 12/1/98

Redacted 2

pages of trade

secret and/or

confidential

commercial

information